Race, ethnicity, and cognition in persons newly diagnosed with multiple sclerosis

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Abstract

Objective

To determine whether black or Hispanic patients with newly diagnosed multiple sclerosis (MS) are more likely to have cognitive impairment than white patients when compared to controls matched on age, sex, and race/ethnicity. Whether black or Hispanic patients have a more aggressive MS disease course than white patients remains unclear. No prior studies have examined differences in early cognitive impairment. The oral Symbol Digit Modalities Test (SDMT) is sensitive to early cognitive impairment in MS but normative data in nonwhite patients are limited.

Methods

We studied 1,174 adults who enrolled in the MS Sunshine Study. SDMT and verbal fluency were measured in 554 incident cases of MS or clinically isolated syndrome (CIS) and 620 matched controls. Multivariable regression was used to examine correlates of abnormal SDMT in the entire cohort.

Results

The strongest independent predictors of lower oral SDMT scores in rank order were having MS/CIS, lower educational attainment, and being black or Hispanic. Black and Hispanic patients and controls had lower SDMT scores than white participants even after controlling for age, sex, and education. However, no interaction between race/ethnicity and MS case status on SDMT scores was detected. Easy-to-use reference scores stratified by age and educational attainment for black and Hispanic patients are provided.

Conclusion

Persons with newly diagnosed MS/CIS are more likely to have subtly impaired cognitive function than controls regardless of race/ethnicity. Lower absolute SDMT scores among black and Hispanic patients compared to white patients highlight underlying US population differences rather than differences in MS disease severity.

Glossary

CIS = clinically isolated syndrome; EHR = electronic health record; IQR = interquartile range; KPSC = Kaiser Permanente Southern California; MS = multiple sclerosis; SDMT = Symbol Digit Modalities Test.

Multiple sclerosis (MS) is a chronic inflammatory CNS disease that often triggers neurodegenerative changes early in the disease course. Over time, most patients with MS accrue irreversible physical or cognitive disability, or both. Identifying patients at high risk for future disability can be used to target interventions to prevent further inflammation and neurodegeneration and improve cognition.

Subtle cognitive impairment has been described in referral center populations¹ early in MS and predicts disabling cognitive impairment later on in the disease course.^{2,3} Whether early cognitive impairment in MS varies by race/ethnicity is unknown. Some authors have suggested that black patients^{4,5} and perhaps Hispanic patients with MS have a worse prognosis than white patients,⁶ but these studies focused only on physical disability and had other important limitations including referral center bias,⁴⁻⁶ cross-sectional assessment of prevalent cases,⁴⁻⁶ and lack of adjustment for socioeconomic status⁴⁻⁶ that can lead to overestimation of racial differences.⁷

The Symbol Digit Modalities Test (SDMT) is a sensitive and reliable measure of early cognitive impairment in MS⁸ and other neurologic disorders. It assesses attention, processing speed, and working memory and is also sensitive to neurocognitive changes over time.⁸ The oral version of the SDMT also circumvents the effect of potentially impaired hand function on scores. This, along with the ease of administration and scoring, has made the oral SDMT the preferred cognitive assessment tool in MS clinics.

Straightforward normative values appropriate for use in clinical practice are readily available from large white cohorts⁹⁻¹¹ but are limited for black and Hispanic patients. This is important because several non-MS studies have shown that race and ethnicity affect SDMT scores independent of readily measurable sociodemographic factors.^{12,13} These differences are primarily due to pervasive disparities between racial and ethnic groups yet have broad influences on many aspects of performance including neuropsychological assessments, rather than innate differences in cognitive abilities. Thus when we measure SDMT in black and Hispanic patients with MS, comparing the results to normative values in white patients would likely lead to the incorrect conclusion that there are innate or disease-induced differences in cognitive abilities.

The goal of the analyses presented herein was to utilize data from the MS Sunshine study to determine whether black or Hispanic patients with MS have more cognitive impairment early in the disease course than white patients when compared to appropriate controls. In addition, we provide reference

values obtained from black and Hispanic controls that can be used in daily clinical practice.

Methods

Primary study population

Kaiser Permanente Southern California (KPSC) is a large health maintenance organization with over 4 million members representative of the general population in Southern California.¹⁴ KPSC uses an integrated electronic health record (EHR) system that includes all inpatient and outpatient encounters, diagnostic tests, diagnoses, and medications, and some demographic and behavioral characteristics.

Participants in the MS Sunshine Study were identified and recruited from the KPSC membership between December 2011 and December 2014 as described previously.¹⁵ Data were collected from the structured in-person interview and EHR. Briefly, potentially eligible incident cases were identified via the EHR; eligibility and diagnosis of MS (according to 2010 McDonald Criteria¹⁶ or clinically isolated syndrome [CIS]^{17,18}) was confirmed by an MS specialist (A.L.-G.) prior to recruitment for an in-person study visit. All of the participants classified as CIS at the time this study was conducted would be classified as MS according to the 2017 MS diagnostic criteria,¹⁹ and are henceforth referred to as newly diagnosed MS.

At least 1 control participant from the KPSC population, matched to the patient on race/ethnicity, birth date (within 2 years), sex, and KPSC facility (a surrogate measure for socioeconomic status), was identified from the EHR and recruited. The controls were assigned the same index date as their matched case (symptom onset date). Detailed participation rates have been described previously.¹⁵

Standard protocol approvals, registrations, and patient consents

The study protocol was approved by the KPSC institutional review board. Written informed consent was obtained from all participants.

Data collection

The oral SDMT was administered in English or Spanish according to the participant's language preference during a structured in-person assessment by trained bilingual study personnel. Covariates obtained from the in-person interview included education, household income, and self-identified race/ethnicity of the participant. Race/ethnicity of the 4 grandparents was used to assess logical consistency and rarely

differed from self-reported race/ethnicity. White, non-Hispanic participants were classified as white; any black race regardless of ethnicity was classified as black; and those who identified themselves as white and Hispanic were classified as Hispanic.

Statistical analyses

SDMT results were available on 1,174 (98.9%) of the 1,187 participants who had completed the study protocol by June 2, 2015. The final analysis cohort included the 1,174 participants who completed the SDMT: 261 black, 394 Hispanic, and 519 white. Participants who declined to provide household income information ($n = 62$) were excluded from multivariable models but retained for the descriptive tables.

Multivariate linear regression was used to evaluate the associations of race/ethnicity and MS with SDMT scores after adjusting for age at interview date, sex, education, and household income ($\geq$ or $<$ \$65,000, the median for California). Education was classified into 3 groups in accordance with the distribution of educational attainment in the United States²⁰ as follows: (1) trade school, completed high school or less; (2) some college but did not complete; or (3) completed 4-year college or higher. To determine whether the black or Hispanic patients with MS have more cognitive impairment than white patients, we tested for a multiplicative interaction between race/ethnicity and having MS. Significance threshold was set at $p < 0.05$.

Sensitivity analyses included multivariable linear regression models stratified by case or control status to assess for potential differences in magnitudes of effect of race/ethnicity on SDMT scores. We also examined whether SDMT performance varied by the language (Spanish vs English) requested by Hispanic participants in additional sensitivity analyses.

Chi-square and Fisher Exact tests were used to compare the frequencies of binary variables, 2-sample t tests were used to compare means, and Wilcoxon rank sum test was used to compare non-normally distributed variables between cases and controls. All analyses were conducted using SAS software v9.4 (Cary, NC).

Data availability

Per KPSC's institutional review board, deidentified data will be available upon reasonable request.

Results

Demographic characteristics and SDMT scores stratified by race/ethnicity of cases and controls are presented in table 1. Of the 1,174 participants, most were female (71%), with a mean age of 40.7 years at the time of cognitive testing. The majority of Hispanic participants were of Mexican (78.9%) or mixed-Mexican descent (3.4%) and the majority of black participants (97.2%) were African Americans born in the United States. The median (interquartile range [IQR]) time from diagnosis to cognitive testing among cases was similar between racial/ethnic

groups (white, 10.3 months [IQR, 6.2–14.3]; black, 10.2 months [IQR, 5.4–15.0]; and Hispanic, 10.6 months [IQR, 7.6–17.3]). Fewer black patients with MS/CIS completed college compared to white and Hispanic patients ($p < 0.0001$). Significantly more white patients with MS/CIS (64%) reported an annual household income above the California median (\$65,000) than black (43%) or Hispanic (44%) patients ($p < 0.0001$).

Patients had lower SDMT scores compared to controls across all racial/ethnic groups (table 1 and figure). Black followed by Hispanic patients and controls had lower average SDMT scores compared to white patients and controls, respectively (table 1 and figure).

Table 2 shows the results of multivariable linear regression analyses estimating the independent relationships between race/ethnicity and having MS on SDMT. The effect of being black ($\beta = -5.97$) on predicted SDMT score is similar to having MS ($\beta = -6.04$), followed by very low educational attainment ($\beta = -5.02$), being Hispanic ($\beta = -3.06$), and each increasing 10 years of age ($\beta = -3.03$). No significant interaction between race/ethnicity and having MS on SDMT scores was detected ($p = 0.41$).

Sensitivity analyses (table 2) examining the relationship between race/ethnicity and SDMT scores in patients or controls separately show that being black or Hispanic is associated with similarly reduced SDMT scores in patients and controls (-6.55 , -5.66 , -2.21 , and -3.86 for black or Hispanic patients and controls, respectively).

Among Hispanic participants, 23 participants (8 cases and 15 controls) requested administration of the questionnaire and SDMT in Spanish. Spanish language preference was independently associated with a lower SDMT score compared to Hispanic participants with English language preference (table 3).

Easy-to-use normative SDMT values stratified by age and educational attainment are provided for each racial/ethnic group in table 4.

Discussion

We did not find any evidence that MS causes more cognitive impairment in black or Hispanic patients early in the disease course compared to white patients. We found that cognitive performance as measured by the oral SDMT was lower in black and Hispanic patients newly diagnosed with MS/CIS compared to white patients, but that this is attributable to underlying population differences rather than MS disease severity. Consistent with previous non-MS studies,^{12,13} we found that black and Hispanic controls have lower SDMT scores than white controls even after accounting for age, sex, education, and income. Our findings underscore the importance of comparing SDMT results in patients to normative values from the appropriate racial/ethnic group before drawing conclusions about

Table 1 Demographic information and neurocognitive scores for the multiethnic multiple sclerosis cohort and controls

	White participants			Black participants			Hispanic participants			Total		
	Cases (n = 245)	Controls (n = 274)	p Value	Cases (n = 121)	Controls (n = 140)	p Value	Cases (n = 188)	Controls (n = 206)	p Value	Cases (n = 554)	Controls (n = 620)	p Value
Age at interview, y, mean (SD)	43.3 (12.2)	44.2 (12.2)	0.370	41.7 (12.7)	42.3 (12.7)	0.608	35.5 (11.0)	36.0 (11.0)	0.598	40.3 (12.4)	41.1 (12.5)	0.277
Female, n (%)	164 (66.9)	179 (65.3)	0.699	95 (78.5)	107 (76.4)	0.688	135 (71.8)	152 (73.8)	0.659	394 (71.1)	438 (70.6)	0.858
Education, n (%)												
Technical school or lower	36 (14.7)	43 (15.7)	0.019	25 (20.7)	21 (15.0)	0.444	67 (35.6)	68 (33.0)	0.493	128 (23.1)	132 (21.3)	0.234
Some college	96 (39.2)	76 (27.7)		44 (36.4)	51 (36.4)		64 (34.0)	82 (39.8)		204 (36.8)	209 (33.7)	
Complete college or higher	113 (46.1)	155 (56.6)		52 (43.0)	68 (48.6)		57 (30.3)	56 (27.2)		222 (40.1)	279 (45.0)	
Annual household income, n (%)												
\$65,000 or less	76 (31.0)	68 (24.8)	0.115	62 (51.2)	70 (50.0)	0.736	94 (50.0)	100 (48.5)	0.682	232 (41.9)	238 (38.4)	0.183
\$65,001 or more	157 (64.1)	192 (70.1)		52 (43.0)	64 (45.7)		82 (43.6)	95 (46.1)		291 (52.5)	351 (56.6)	
Declined	12 (4.9)	14 (5.1)		7 (5.8)	6 (4.3)		12 (6.4)	11 (5.3)		31 (5.6)	31 (5.0)	
Cognitive test scores												
Oral SDMT, mean (SD)	54.0 (12.8)	60.5 (10.1)	<0.0001	47.3 (12.5)	54.8 (10.7)	<0.0001	53.0 (11.6)	57.7 (10.7)	<0.0001	52.2 (12.6)	58.3 (10.6)	<0.0001

Abbreviation: SDMT = Symbol Digit Modalities Test.

Figure Distribution of Symbol Digit Modalities Test (SDMT) scores by race/ethnicity among controls and patients with newly diagnosed multiple sclerosis

Depicted are Gaussian distributions of the unadjusted SDMT scores among white participants (in blue), Hispanic participants (in green), and black participants (in red) among controls (A) and cases (B). The curves are shifted to the left depicting lower scores among cases compared to controls for all racial/ethnic groups ($p < 0.001$ for all comparisons). In both panels, the curves are shifted to the left for black participants, and to a lesser extent for Hispanic compared to white participants.

racial/ethnic differences in disease severity. Taken together with findings from other non-MS studies, these findings also highlight a troubling societal problem in the United States.

Little is known about racial/ethnic influences on cognitive impairment in MS. Only 2 studies^{21,22} with significant limitations including selection bias,^{21,22} cross-sectional design,²² and small sample²² have addressed this question in black patients and none, to our knowledge, in Hispanic patients. Both studies, one in nursing home residents with MS²¹ and

another in pediatric-onset MS,²² observed lower cognitive performance in black compared to white patients as we did, but neither compared results to ethno-specific norms. Nationality (Brazil, Argentina, United States, Iran, or Czech Republic) has been independently associated with performance on the brief international cognitive assessment for MS,²³ a battery of tests that includes the oral SDMT. Whether this is consistent with our findings is unclear, as they did not specifically measure race or ethnicity or report which nationalities scored higher or lower.²³ However, it does highlight

Table 2 Predictors of Symbol Digit Modalities Test scores in patients with newly diagnosed multiple sclerosis and controls

	Total (n = 1,112) ^a			Controls (n = 589)			Cases (n = 523)		
	β	SE	p Value	β	SE	p Value	β	SE	p Value
Intercept	76.45	1.39	<0.0001	76.09	1.67	<0.0001	70.6	2.17	<0.0001
Age	-0.303	0.03	<0.0001	-0.31	0.03	<0.0001	-0.29	0.04	<0.0001
Male sex	-1.50	0.7	0.032	1.01	0.86	0.2414	-4.38	1.12	0.0001
Education (reference college or higher)									
Some college	-2.39	0.73	0.0011	-1.75	0.90	0.0530	-2.87	1.17	0.0149
High school, trade school, or less	-5.02	0.87	<0.0001	-4.89	1.08	<0.0001	-5.27	1.37	0.0001
Household income ≤\$65,000	-2.28	0.67	0.0007	-2.32	0.84	0.0059	-2.03	1.07	0.0578
Race/ethnicity (reference white)									
Hispanic	-3.06	0.78	<0.0001	-3.86	0.98	<0.0001	-2.21	1.24	0.0758
Black	-5.97	0.84	<0.0001	-5.66	1.03	<0.0001	-6.55	1.35	<0.0001
Multiple sclerosis	-6.04	0.63	<0.0001	NA			na		

^a A total of 62 participants had unknown/declined to answer for income.

Table 3 Role of Spanish-language preference on Symbol Digit Modalities Test (SDMT) scores among Hispanic participants

	Total (n = 371) ^a		
	β	SE	p Value
Intercept	72.72	2.24	<0.0001
Age	-0.30	0.05	<0.0001
Male sex	1.33	1.21	0.2707
Education (reference college or higher)			
Some college	-3.33	1.33	0.0128
High school, trade school, or less	-5.15	1.40	0.0003
Household income $\leq$ \$65,000	-2.07	1.09	0.0593
SDMT in Spanish ^b	-6.11	2.40	0.0114
Multiple sclerosis	-5.07	1.07	<0.0001

^a A total of 23 participants had unknown/declined to answer for income (1 of whom had SDMT completed in Spanish).

^b Compared to English-language preference.

that comparison to appropriate norms is important before drawing conclusions about differences in disease severity. Without appropriate normative values, our results could have easily been misinterpreted as evidence that black patients followed by Hispanic patients have a more aggressive MS disease course even less than 1 year after diagnosis.

Our results are consistent with modifiable and nonmodifiable sociodemographic variables that have been shown to independently affect SDMT scores in non-MS populations.^{10,12} Similar to non-MS populations, we found that modifiable factors, higher household income and educational attainment, are associated with better cognitive performance across all racial/ethnic groups independent of disease state, as are nonmodifiable factors (such as younger age).^{10,12,13} It is thus troubling that black patients and Hispanic patients newly diagnosed with MS in our study had lower educational attainment and more lived in households with incomes below the California state median compared to white patients. This is consistent with racial/ethnic disparities in education and income across the United States.

Racial, ethnic, and cultural differences in cognitive tests including SDMT have long been recognized.^{13,24–26} Black and Hispanic participants typically score lower than white participants in US studies, particularly on tests influenced by reading level but also on SDMT.^{13,25} Indigenous Australians score lower on the SDMT than white Australians¹⁰ and black participants of Caribbean ethnicity scored lower than African Americans independent of sociodemographic factors in a large US study.¹²

Baseline differences in performance on neuropsychological tests should not be interpreted as innate differences in intellectual ability between groups. Pervasive racial and ethnic disparities can affect performance on neuropsychological tests

by depriving groups of reaching their full potential through lower quality of education²⁷ and more early life stressors.²⁸ Racially driven political malaise that results in unnecessary and prolonged exposure of minorities to neurotoxins like lead^{29,30} also contributes. In addition, there are factors that simply influence test-taking ability that disproportionately affect minorities. These include test anxiety from stereotype threat related to their intellect³¹ and cultural differences like placing little value on speediness.³² The lower SDMT scores in only-Spanish-speaking Hispanic participants we observed are best explained by a combination of these factors. However, we did not measure these or other, often overlapping factors, thus to what extent they affect the differences in oral SDMT scores observed in our study and others^{10,12,13} is unknown. This is the main limitation of our study.

While representative of Californians, another limitation of our study is the lack of ethnic diversity among Hispanic or black participants, relatively few SDMTs administered in Spanish, and lack of information on bilingualism. Thus it is unclear whether our normative values are generalizable to black participants of Caribbean ethnicity, recent African immigrants, non-Mexican Hispanic participants, or bilingual English–Spanish speakers. In addition, because we matched controls to incident cases, our study includes relatively few men and elderly subjects. Therefore, we could not stratify normative values by sex, as has been done in large population-based samples,¹⁰ and normative values in older patients and those with very low educational attainment are based on small samples. These normative tables should be augmented with larger samples in future studies.

Furthermore, we measured oral SDMT at only one time point shortly after diagnosis, and thus cannot exclude the possibility of differential decline across race/ethnicity at later stages of the disease. This is plausible, not so much because there is strong evidence of inherent differences in MS disease severity, but because of marked racial/ethnic disparities in US health care access and utilization³³ that can lead to lack of a timely diagnosis and access to disease-modifying treatments.

The strengths of this study include the clinical importance of the question, the relatively large sample of incident cases accrued over a relatively short period of time, and recruitment of matched controls from a population-based cohort. Other strengths include the use of a clinically scalable test and providing easy-to-use normative values that, although imperfect, can serve as a more accurate starting point to identify black and Hispanic patients with MS with cognitive impairment.

Taken together, the findings from this and previous studies can be used to guide recommendations to potentially prevent lower cognitive performance in patients with MS both in the clinic and from a societal perspective. We provide normative SDMT values for Hispanic and black participants in the United States in age ranges typical of newly diagnosed patients with MS that can help clinicians identify patients with MS with cognitive impairment who may benefit from interventions. In addition to

Table 4 Normative data for oral Symbol Digit Modalities Test stratified by age and education level in white, Hispanic, and black controls

Age at interview, y	High school, trade school or less						Some college						Completed 4-year college or higher					
	No.	Mean	SD	25th percentile	50th percentile	75th percentile	No.	Mean	SD	25th percentile	50th percentile	75th percentile	No.	Mean	SD	25th percentile	50th percentile	75th percentile
White controls																		
19–29	3	60.0	1.0	59.0	60.0	61.0	14	61.4	6.0	57.0	62.5	66.0	20	64.0	10.1	55.0	64.0	70.5
30–39	9	60.4	10.9	56.0	65.0	66.0	11	63.8	11.2	57.0	61.0	75.0	45	65.0	8.3	59.0	67.0	71.0
40–49	13	56.5	7.7	54.0	55.0	64.0	20	63.6	10.3	55.5	61.5	68.5	43	63.0	11.6	57.0	61.0	67.0
50–59	10	56.6	6.6	50.0	57.0	61.0	19	54.9	9.7	49.0	56.0	61.0	35	58.5	8.2	52.0	59.0	63.0
60–69	8	51.6	13.6	43.5	56.0	61.5	10	53.2	10.0	44.0	50.5	64.0	10	56.3	7.1	50.0	56.5	63.0
Black controls																		
19–29	4	42.8	14.0	34.5	48.5	51.0	12	63.3	10.6	57.0	65.0	68.0	10	62.5	10.5	52.0	60.5	74.0
30–39	7	56.0	6.6	51.0	57.0	61.0	11	57.9	10.4	51.0	59.0	64.0	19	60.5	10.7	54.0	63.0	68.0
40–49	5	46.4	5.5	47.0	47.0	50.0	16	50.8	9.3	43.5	52.0	57.5	15	58.5	7.4	51.0	62.0	64.0
50–59	2	44.0	4.2	41.0	44.0	47.0	7	49.9	8.2	44.0	50.0	58.0	17	50.9	9.5	45.0	50.0	58.0
60–69	2	45.0	5.7	41.0	45.0	49.0	3	51.3	12.9	37.0	55.0	62.0	7	48.3	5.8	42.0	50.0	51.0
Hispanic controls																		
19–29	17	60.2	8.0	55.0	59.0	63.0	34	61.8	11.0	55.0	63.0	69.0	16	65.2	8.0	58.5	66.5	70.5
30–39	20	52.7	9.4	47.0	51.5	59.0	25	58.5	9.0	52.0	57.0	67.0	23	60.7	7.9	55.0	61.0	66.0
40–49	19	54.5	10.0	46.0	55.0	62.0	20	55.9	10.3	50.0	54.5	60.0	7	61.0	17.2	48.0	57.0	79.0
50–59	8	47.6	11.2	38.0	52.5	55.5	1	.	.	.	.	.	9	52.9	6.7	51.0	53.0	58.0
60–69	3	38.0	12.3	24.0	43.0	47.0	2	50.5	6.4	46.0	50.5	55.0	1	.	.	.	.	.

optimizing MS disease-modifying treatments to slow cognitive decline, interventions aimed at improving cognition may also be beneficial. Observational studies point to options like mentally stimulating hobbies³⁴ and decreasing neuroticism,³⁵ as well as recommendations with known general health benefits including exercise, preventing obesity, and hypertension.³⁴ From a societal perspective, improving opportunities for higher educational attainment and higher incomes for black and Hispanic participants in the United States would likely reduce racial/ethnic disparities in cognitive performance.

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Edlin G. Gonzales, MA	Kaiser Permanente Southern California, Pasadena	Collected data, revised the manuscript for content
Samantha Haraszti, MS	Philadelphia College of Osteopathic Medicine, Pennsylvania	Collected data, revised the manuscript for content
Annette Langer-Gould, MD, PhD	Los Angeles Medical Center, Department of Neurology, Southern California Permanente Medical Group	Designed and conceptualized study, collected and interpreted the data, drafted and revised the manuscript for intellectual content, had full access to all the data and takes responsibility for the integrity of the data and accuracy of the data analysis

References

- Anhoque CF, Domingues SCA, Teixeira AL, Domingues RB. Cognitive impairment in clinically isolated syndrome: a systematic review. *Dement Neuropsychol* 2010;4:86–90.
- Amato MP, Ponziani G, Pracucci G, Bracco L, Siracusa G, Amaducci L. Cognitive impairment in early-onset multiple sclerosis: pattern, predictors, and impact on everyday life in a 4-year follow-up. *Arch Neurol* 1995;52:168–172.
- Kujala P, Portin R, Ruutinen J. The progress of cognitive decline in multiple sclerosis: a controlled 3-year follow-up. *Brain* 1997;120:289–297.
- Weinstock-Guttman B, Jacobs LD, Brownschield CM, et al. Multiple sclerosis characteristics in African American patients in the New York State Multiple Sclerosis Consortium. *Mult Scler* 2003;9:293–298.
- Cree BA, Khan O, Bourdette D, et al. Clinical characteristics of African Americans vs Caucasian Americans with multiple sclerosis. *Neurology* 2004;63:2039–2045.
- Ventura RE, Antezana AO, Bacon T, Kister I. Hispanic Americans and African Americans with multiple sclerosis have more severe disease course than Caucasian Americans. *Mult Scler* 2017;23:1554–1557.
- Marrie RA, Cutter G, Tyry T, Vollmer T, Campagnolo D. Does multiple sclerosis-associated disability differ between races? *Neurology* 2006;66:1235–1240.
- Benedict RH, DeLuca J, Phillips G, et al. Validity of the Symbol Digit Modalities Test as a cognition performance outcome measure for multiple sclerosis. *Mult Scler* 2017;23:721–733.
- Nocentini U, Giordano A, Di Vincenzo S, Panella M, Pasqualetti P. The Symbol Digit Modalities Test: oral version: Italian normative data. *Funct Neurol* 2006;21:93–96.
- Kiely KM, Butterworth P, Watson N, Wooden M. The Symbol Digit Modalities Test: normative data from a large nationally representative sample of Australians. *Arch Clin Neuropsychol* 2014;29:767–775.
- Arango-Lasprilla JC, Rivera D, Trapp S, et al. Symbol Digit Modalities Test: normative data for Spanish-speaking pediatric population. *NeuroRehabilitation* 2017;41:639–647.
- Gonzalez HM, Whitfield KE, West BT, Williams DR, Lichtenberg PA, Jackson JS. Modified-Symbol Digit Modalities Test for African Americans, Caribbean black Americans, and non-Latino whites: nationally representative normative data from the National Survey of American Life. *Arch Clin Neuropsychol* 2007;22:605–613.
- Manly JJ, Smith C, Crystal HA, et al. Relationship of ethnicity, age, education, and reading level to speed and executive function among HIV+ and HIV- women: the Women's Interagency HIV Study (WIHS) Neurocognitive Substudy. *J Clin Exp Neuropsychol* 2011;33:853–863.
- Koebnick C, Langer Gould A, Gould MK, et al. Do the sociodemographic characteristics of members of a large, integrated health care system represent the population of interest? *Permanente J* 2012;16:37–41.
- Langer-Gould A, Lucas R, Xiang AH, et al. MS Sunshine Study: sun exposure but not vitamin D is associated with multiple sclerosis risk in blacks and Hispanics. *Nutrients* 2018;10:E268.
- Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol* 2011;69:292–302.
- Transverse Myelitis Consortium Working Group. Proposed diagnostic criteria and nosology of acute transverse myelitis. *Neurology* 2002;59:499–505.
- Jacob A, Weinshenker BG. An approach to the diagnosis of acute transverse myelitis. *Semin Neurol* 2008;28:105–120.
- Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol* 2018;17:162–173.
- US Census Bureau. Educational Attainment in the United States: 2014. Available at: <https://census.gov/data/tables/2014/demo/educational-attainment/cps-detailedtables.html>. Accessed April 15, 2019.
- Buchanan RJ, Martin RA, Wang S, Kim M. Racial analyses of longer-stay nursing home residents with multiple sclerosis. *Ethn Dis* 2006;16:159–165.
- Ross KA, Schwebel DC, Rinker J II, Ness J, Ackerson J. Neurocognitive sequelae in African American and Caucasian children with multiple sclerosis. *Neurology* 2010;75:2097–2102.
- Smerbeck A, Benedict RHB, Eshaghi A, et al. Influence of nationality on the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS). *Clin Neuropsychol* 2018;32:54–62.
- Manly JJ, Jacobs DM, Sano M, et al. African American acculturation and neuropsychological test performance among nondemented community elders. *J Int Neuropsychol Soc* 1998a;4:77.
- Manly JJ, Jacobs DM, Sano M, et al. Cognitive test performance among nondemented elderly African Americans and whites. *Neurology* 1998;50:1238–1245.
- Baird AD, Ford M, Podell K. Ethnic differences in functional and neuropsychological test performance in older adults. *Arch Clin Neuropsychol* 2007;22:309–318.
- Manly JJ, Jacobs DM, Touradj P, Small SA, Stern Y. Reading level attenuates differences in neuropsychological test performance between African American and White elders. *J Int Neuropsychol Soc* 2002;8:341–348.
- Saleh A, Potter GG, McQuoid DR, et al. Effects of early life stress on depression, cognitive performance and brain morphology. *Psychol Med* 2017;47:171–181.
- Ruckart PZ, Ettinger AS, Hanna-Attisha M, Jones N, Davis SI, Breyse PN. The Flint Water crisis: a coordinated public health emergency response and recovery initiative. *J Public Health Manag Pract* 2019;25(suppl 1):S84–S90.

30. Whitehead LS, Buchanan SD. Childhood lead poisoning: a perpetual environmental justice issue? *J Public Health Manag Pract* 2019;25(suppl 1):S115–S120.
31. Chasteen AL, Bhattacharyya S, Horhota M, Tam R, Hasher L. How feelings of stereotype threat influence older adults' memory performance. *Exp Aging Res* 2005;31:235–260.
32. Ardila A. Cultural values underlying psychometric cognitive testing. *Neuropsychol Rev* 2005;15:185–195.
33. Bor J, Cohen GH, Galea S. Population health in an era of rising income inequality: USA, 1980-2015. *Lancet* 2017;389:1475–1490.
34. Sumowski JF. Cognitive reserve as a useful concept for early intervention research in multiple sclerosis. *Front Neurol* 2015;6:176.
35. Leavitt VM, Buyukturkoglu K, Inglese M, Sumowski JF. Protective personality traits: high openness and low neuroticism linked to better memory in multiple sclerosis. *Mult Scler* 2017;23:1786–1790.